

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
7 July 2005 (07.07.2005)

PCT

(10) International Publication Number
WO 2005/061474 A1

(51) International Patent Classification⁷: C07D 305/14

(21) International Application Number:
PCT/BR2004/000242

(22) International Filing Date:
10 December 2004 (10.12.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PI0305824-7 12 December 2003 (12.12.2003) BR
Prov.020040015028
8 December 2004 (08.12.2004) BR

(71) Applicants (for all designated States except US):
QUIRAL QUÍMICA DO BRASIL [BR/BR]; Rua José
Lourenço, 245, Bairro São Pedro, 36036-230 Juiz de
Fora (BR). BIORGÂNICA LTDA. [BR/BR]; Rua José
Lourenço, 245, Bairro São Pedro, 36036-230 Juiz de Fora
(BR).

(72) Inventors; and

(75) Inventors/Applicants (for US only): SANTINI, Marco
Antônio [BR/BR]; Rua José Lourenço, 245, Bairro São
Pedro, 36036-230 Juiz de Fora (BR). MACHADO,
Antônio [BR/BR]; Rua José Lourenço, 245, Bairro São
Pedro, 36036-230 Juiz de Fora (BR). MARANDUBA,
Aurélio [BR/BR]; Rua José Lourenço, 245, Bairro São
Pedro, 36036-230 Juiz de Fora (BR). GUIMARÃES,
Eneida [BR/BR]; Rua José Lourenço, 245, Bairro São
Pedro, 36036-230 Juiz de Fora (BR). SANTIAGO
JUNIOR, Marcio [BR/BR]; Rua José Lourenço, 245,

Bairro São Pedro, 36036-230 Juiz de Fora (BR). SILVA,
Maria [BR/BR]; Rua José Lourenço, 245, Bairro São
Pedro, 36036-230 Juiz de Fora (BR). GRAZUL, Richard
[BR/BR]; Rua José Lourenço, 245, Bairro São Pedro,
36036-230 Juiz de Fora (BR).

(74) Agent: LLC INFO CONNECTION LTDA.; 5555 Dom
Hélder Câmara Av., RM 312, Pílares, 20771-001 Rio de
Janeiro - RJ (BR).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, GR, GU, HT, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

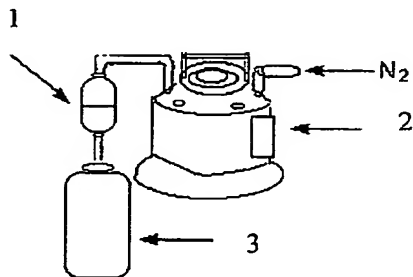
(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,
SE, SI, SK, TR), OAPI (BF, BJ, CI, CG, CL, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: PROCESS FOR THE PREPARATION OF ANHYDROUS AND HYDRATED ACTIVE PHARMACEUTICAL IN-
GREDIENTS (APIS): STABLE PHARMACEUTICAL COMPOSITIONS PREPARED FROM THE SAME AND USES OF SAID
COMPOSITIONS



(57) Abstract: This invention describes a process for the production
of ANHYDROUS active pharmaceutical ingredients (APIs); a process
for the preparation of HYDRATED active pharmaceutical ingredients, a
process for the preparation of sterile and stable injectable solutions, and
their use, more specifically, APIs which are taxane derivatives, especially
(2R,3S) 4-acetoxy-2- α -benzoyloxy-5 β -20-epoxy-1,7- β -10- β -tri-hy-
droxy-9-oxo-tax-11-en-13 α -il 3-tert-butoxycarbonylamino-2-hy-
droxy-3-phenylpropionate (I); 4-acetoxy-2- α -benzoyloxy-5- β -20-epoxy-1,
7 β -10- β -tri-hidroxy-9-oxo-tax-11-en-13 α -il (2R,3S) 3-benzoylamino-2-hy-
droxy-3-phenylpropionate (II), and particularly 4-acetoxy-2- α -benzoy-
loxy-5 β -20-epoxy-1, 7 β -10- β -tri-hidroxy-9-oxo-tax-11-en-13 α -il (2R,3S)
3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate tri-hydrate (III).

BEST AVAILABLE COPY

WO 2005/061474 A1